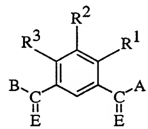
CLAIMS

What is claimed is:

1. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula I



I

wherein:

R^1, R^2, and R^3 independently are hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3;

E is independently O or S;

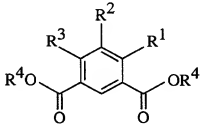
A and B independently are OR^4 or NR^4R^5;

each R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof.

2. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula II



II

wherein:

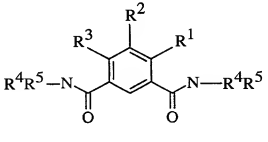
R^1, R^2, and R^3 independently are hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3; and

R^4 and R^5 is independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, or $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof.

3. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula III



III

wherein:

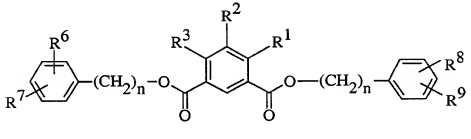
R^1, R^2, and R^3 independently are hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3;

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof.

4. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula IV



IV

wherein:

Each R^1, R^2, and R^3 independently are hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3;

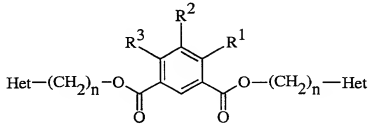
Each R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

R^6, R^7, R^8, and R^9 independently are hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, nitro, or NH_2; and

n is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof.

5. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula V



V

wherein:

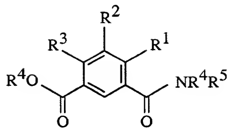
R^1, R^2, and R^3 independently are hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3, and Het is an unsubstituted or substituted heteroaryl group;

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof.

6. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula VI



VI

or a pharmaceutically acceptable salt thereof,

wherein:

R^1, R^2, and R^3 independently are hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3;

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted; and

n is an integer from 0 to 6.

7. A compound selected from:

4-Methoxy-N,N′-bis-(4-methoxybenzyl)-isophthalamide;

Isophthalic acid di-(2,1,3-benzothiadiazol-5-yl) methyl ester;

4-Methoxy-isophthalic acid dibenzyl ester;

4-Methoxy-isophthalic acid dipyridin-4-ylmethyl ester;

Isophthalic acid bis-(4-fluoro-benzyl) ester;

Isophthalic acid bis-(3-fluoro-benzyl) ester;

Isophthalic acid bis-(4-methoxy-benzyl) ester;

Isophthalic acid bis-(3-methoxy-benzyl) ester;

Isophthalic acid bis-(1,3-benzodioxol-5-ylmethyl) ester;

N,N′-Bis-(3-fluoro-benzyl)-isophthalamide;

4-Acetyl-isophthalic acid dibenzyl ester;

4-Methoxycarbonylmethoxy-isophthalic acid dibenzyl ester;

N,N′-Bis-1,3-benzodioxol-5-ylmethyl-4-methoxy-isophthalamide;

N-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N′-(4-methoxy-benzyl)-isophthalamide;

4-Methoxy-N,N′-bis-(4-methoxy-benzyl)-isophthalamide;

N-1,3-Benzodioxol-5-ylmethyl-N′-(4-chloro-benzyl)-4-methoxy-isophthalamide;

N-Benzyl-4-methoxy-N′-(4-methoxy-benzyl)-isophthalamide;

N′-Benzyl-4-methoxy-N-(4-methoxy-benzyl)-isophthalamide;

4-Methoxy-N-(4-methoxy-benzyl)-N′-pyridin-4-ylmethyl-isophthalamide;

N′-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N-(2-phenoxy-ethyl)-isophthalamide;

N-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N′-(2-phenoxy-ethyl)-isophthalamide;

N-1,3-Benzodioxol-5-ylmethyl-N′-furan-2-ylmethyl-isophthalamide;

N′-1,3-Benzodioxol-5-ylmethyl-N-(2-ethoxy-ethyl)-4-methoxy-isophthalamide;

N,N′-Bis-(3-hydroxymethyl-phenyl)-isophthalamide;

N-Benzyl-4-methoxy-N′-(2-phenoxy-ethyl)-isophthalamide;

4-Methoxy-N,N′-bis-(4-methyl-benzyl)-isophthalamide;

4-Methoxy-N,N′-bis-(3-methoxy-benzyl)-isophthalamide;

N-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N′-(4-methoxy-benzyl)-isophthalamide;

N-1,3-Benzodioxol-5-ylmethyl-isophthalamic acid, (4-carboxyphenyl)methyl ester;

4-{[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]-methyl}-benzoic acid;

4-Methoxy-isophthalic acid di-2,1,3-benzothiadiazol-5-ylmethyl ester;

4-{[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]-methyl}-benzoic acid methyl ester;

N-(3-Methoxy-benzyl)-N′-(4-nitro-benzyl)-isophthalamide;

N-(3,4-Dichloro-benzyl)-N′-pyridin-4-ylmethyl-isophthalamide;

N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-ethoxy-isophthalamide;

N-(4-Chloro-benzyl)-N′-(3-methoxy-benzyl)-isophthalamide;

N-(3,4-Dichloro-benzyl)-N′-(3-methoxy-benzyl)-isophthalamide;

N-(4-Methoxy-benzyl)-N′-(3-methoxy-benzyl)-isophthalamide;

N,N′-Bis-(4-fluoro-3-methoxy-benzyl)-isophthalamide;

4-Ethoxy-N1,N3-bis-(3-methoxy-benzyl)-isophthalamide;

N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-ethoxy-isophthalamide;

N-(3-Methoxy-benzyl)-N′-pyridin-3-ylmethyl-isophthalamide;

N-(3-Methoxy-benzyl)-N′-pyridin-4-ylmethyl-isophthalamide;

N1-1,3-Benzodioxol-5-ylmethyl-N3-pyridin-3-ylmethyl-isophthalamide;

N-(3-Methoxy-benzyl)-N′-(3-trifluoromethoxy-benzyl)-isophthalamide;

N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-isopropoxy-isophthalamide;

4-Isopropoxy-N1,N3-bis-(3-methoxy-benzyl)-isophthalamide;

N1-Benzyl-4-methoxy-N3-(4-methoxy-benzyl)-isophthalamide;

N1-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N3-(4-methoxy-benzyl)-isophthalamide;

N1-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N3-(2-phenoxy-ethyl)-isophthalamide;

N1-Benzyl-4-methoxy-N3-(2-phenoxy-ethyl)-isophthalamide;

N1-1,3-Benzodioxol-5-ylmethyl-N3-(4-chloro-benzyl)-4-methoxy-isophthalamide;

N3-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N1-(4-methoxy-benzyl)-isophthalamide;

N3-Benzyl-4-methoxy-N1-(4-methoxy-benzyl)-isophthalamide;

N3-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N1-(2-phenoxy-ethyl)-isophthalamide;

N3-1,3-Benzodioxol-5-ylmethyl-N1-(2-ethoxy-ethyl)-4-methoxy-isophthalamide;

4-Methoxy-N1-(4-methoxy-benzyl)-N3-pyridin-4-ylmethyl-isophthalamide;

4-Amino-N1,N3-bis-1,3-benzodioxol-5-ylmethyl-isophthalamide;

4-Acetylamino-N1,N3-bis-1,3-benzodioxol-5-ylmethyl-isophthalamide;

N-(3-Methoxy-benzyl)-N′-pyridin-3-ylmethyl-isophthalamide;

N-(3-Methoxy-benzyl)-N′-pyridin-4-ylmethyl-isophthalamide;

N1-1,3-Benzodioxol-5-ylmethyl-N3-pyridin-3-ylmethyl-isophthalamide;

N-(4-Chloro-benzyl)-N′-(3-methoxy-benzyl)-isophthalamide;

N-(3,4-Dichloro-benzyl)-N′-(3-methoxy-benzyl)-isophthalamide;

N-(4-Methoxy-benzyl)-N′-(3-methoxy-benzyl)-isophthalamide;

N-(3-Methoxy-benzyl)-N′-(4-methyl-benzyl)-isophthalamide;

N,N′-Bis-(4-fluoro-3-methoxy-benzyl)-isophthalamide;

({3-[(1,3-Benzodioxol-5-ylmethyl)-carbamoyl]-benzoyl}-benzyl-amino)-acetic acid;

N-Benzo[1,3]dioxol-5-ylmethyl-isophthalamic(4-hydroxymethyl-benzoic acid) ester;

N-(3,4-Dichloro-benzyl)-N′-pyridin-4-ylmethyl-isophthalamide;

N-(3-Methoxy-benzyl)-N′-(4-nitro-benzyl)-isophthalamide;

4-{[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]-methyl}-benzoic acid methyl ester;

N-3-methoxybenzyl-isophthalamic(4-hydroxymethyl-benzoic acid) ester;

4-{[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]-methyl}-benzoic acid;

N-(3-Amino-benzyl)-N′-(3-methoxy-benzyl)-isophthalamide;

N-(3-Methoxy-benzyl)-N′-(3-nitro-benzyl)-isophthalamide;

4-Ethoxy-N′1,N″3-bis-(3-methoxy-benzyl)-isophthalamide;

N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-ethoxy-isophthalamide;

N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-propoxy-isophthalamide;

N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-isopropoxy-isophthalamide;

N1,N3-Bis-2,1,3-benzothiadiazol-5-ylmethyl-4-methoxy-isophthalamide; and

4-Methoxy-isophthalic acid di-2,1,3-benzothiadiazol-5-ylmethyl ester.

8. A pharmaceutical composition, comprising a compound of Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, diluent, or excipient.

9. A pharmaceutical composition for inhibiting MMP-13 in a mammal, comprising an MMP-13 inhibiting amount of a compound of Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, diluent, or excipient.

10. A method for inhibiting MMP-13 in an animal, comprising administering to the animal an MMP-13 inhibiting amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

11. A method for treating a disease mediated by an MMP-13 enzyme, comprising administering to a patient suffering from such a disease an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

12. A method for treating a cancer, comprising administering to a patient suffering from such a disease an anticancer effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

13. A method for treating breast carcinoma, comprising administering to a patient suffering from such a disease an anticancer effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

14. A method for treating a rheumatoid arthritis, comprising administering to a patient suffering from such a disease an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

15. A method for treating a osteoarthritis, comprising administering to a patient suffering from such a disease an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

16. A method for treating a heart failure, comprising administering to a patient suffering from such a disease an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

17. A method for treating a inflammation, comprising administering to a patient suffering from such a disease an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.